

## BEST AVAILABLE COPY PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE  
 in its capacity as elected Office

Date of mailing (day/month/year) 20 March 2001 (20.03.01)	
International application No. PCT/US00/06728	Applicant's or agent's file reference 07039/145WO1
International filing date (day/month/year) 15 March 2000 (15.03.00)	Priority date (day/month/year) 15 March 1999 (15.03.99)
Applicant CONOVER, Cheryl, A. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
 12 October 2000 (12.10.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Claudio Borton Telephone No.: (41-22) 338.83.38
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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/06728

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 39/395, C12Q 1/00, C12Q 1/68, C12N 9/00

US CL : 424/146.1, 435/4, 435/6, 435/183

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/146.1, 435/4, 435/6, 435/183

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
STN, EAST

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	WO 99/32620 A1 (FORSSMANN et al) 01 July 1999 (01.07.99), p.26.	1-13,33-36
A	SEPPALA, M. et al. Pregnancy proteins in seminal plasma, seminal vesicles, preovulatory follicular fluid, and ovary. Annals of the New York Academy of Sciences. 1985, Vol. 442, pages 212-226, especially pages 219-224.	1,2,4,6-8
A	BERSINGER, N. et al. The pattern of serum levels of pregnancy - associated plasma protein A (PAPP-A) during the ovulatory menstrual cycle. British Journal of Obstetrics and Gynaecology. December 1984, Vol. 91, No. 12, pages 1245-1248, especially page 1246.	1,2,4,6-9
A	SJOBERG, J. et al. Hyperstimulated human preovulatory follicular fluid, luteinized cells of unruptured follicles, and corpus luteum contain pregnancy-associated protein A. Fertility and Sterility. April 1984, Vol. 41, No. 4, pages 551-557, especially pages 553-557.	1,2,4,6-9
Y	BISCHOF, P. et al. Is pregnancy-associated plasma protein A a tumor marker? American Journal of Obstetrics and Gynecology. 15 June 1982 (15.06.1982) Vol. 143, No. 4, pages 379-381, especially page 380.	1-13
Y	KUHADJA, F. et al. Pregnancy-associated plasma protein A. American Journal of Pathology. November 1985, Vol. 121, No. 2, pages 343-348, especially pages 342-347.	1-13

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

01 May 2000 (01.05.2000)

Date of mailing of the international search report

23 MAY 2000

Name and mailing address of the ISA/US

Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

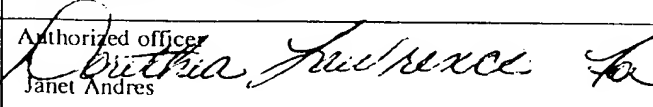
Hurtzell Paula

Telephone No. 703-308-0196

# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 07039/145WO1	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/06728	International filing date (day/month/year) 15 March 2000 (15.03.2000)	Priority date (day/month/year) 15 March 1999 (15.03.1999)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 39/395; C12Q 1/00, 1/68; C12N 9/00 and US Cl.: 424/146.1; 435/4, 6, 183		
Applicant MAYO FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>3</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>0</u> sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>		
Date of submission of the demand 12 October 2000	Date of completion of this report 13 June 2001 (13.06.2001)	
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer  Janet Andres Telephone No. 703-308-0196	

**I. Basis of the report**

## 1. With regard to the elements of the international application:\*

- ☒ the international application as originally filed.
- ☒ the description:  
pages 1-38 as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the claims:  
pages 39-42, as originally filed  
pages NONE, as amended (together with any statement) under Article 19  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the drawings:  
pages 1-5, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the sequence listing part of the description:  
pages 1-5, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.  
These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in printed form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

Novelty (N)	Claims <u>1-36</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>3 and 14-36</u>	YES
	Claims <u>1, 2, 4-13</u>	NO
Industrial Applicability (IA)	Claims <u>1-36</u>	YES
	Claims <u>NONE</u>	NO

**2. CITATIONS AND EXPLANATIONS (Rule 70.7)**

Claims 1, 2, and 4-13 lack an inventive step under PCT Article 33(3) as being obvious over KUHADJA et al., American Journal of Pathology, 1985, Vol. 121, No. 2, pages 343-348, or BISHOF et al., American Journal of Obstetrics and Gynecology, 1982, Vol. 143, No. 4, pages 379-381. Each of these references teaches PPAP A as a marker for cancer. Thus it would be obvious to detect PPAP A as a way of detecting cancer.

Claims 3 and 14-36 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest PPAP A as an IGFBP-4 specific protease.

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 07039/145WO1	<b>FOR FURTHER ACTION</b>	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, Item 5 below.
International application No. PCT/US00/06728	International filing date ( <i>day/month/year</i> ) 15 March 2000 (15.03.2000)	(Earliest) Priority Date ( <i>day/month/year</i> ) 15 March 1999 (15.03.1999)
Applicant MAYO FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 2 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the Report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item:



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (See Box II).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/06728

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US CL : 424/146.1, 435/4, 435/6, 435/183

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
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Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
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A	SJOBERG, J. et al. Hyperstimulated human preovulatory follicular fluid, luteinized cells of unruptured follicles, and corpus luteum contain pregnancy-associated protein A. Fertility and Sterility. April 1984, Vol. 41, No. 4, pages 551-557, especially pages 553-555.	1,2,4,6-9
Y	BISCHOF, P. et al. Is pregnancy-associated plasma protein A a tumor marker? American Journal of Obstetrics and Gynecology. 15 June 1982 (15.06.1982) Vol. 143, No. 4, pages 379-381, especially page 380.	1-13
Y	KUHADJA, F. et al. Pregnancy-associated plasma protein A. American Journal of Pathology. November 1985, Vol. 121, No. 2, pages 343-348, especially pages 342-347.	1-13



Further documents are listed in the continuation of Box C.



See patent family annex.

Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

01 May 2000 (01.05.2000)

Date of mailing of the international search report

23 MAY 2000

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